

Page 6, delete the fifth paragraph starting on line 27, and replace it with the following paragraph:

Furthermore, U.S. Appln. Nos. 09/257,188 and 09/309,881 disclose penetration enhancers (e.g., removal of superficial layers above the dermis, micropenetration to above the dermis) and targeting of complexed antigen and/or adjuvant in the context of transcutaneous immunization.

IN THE CLAIMS:

Kindly enter the following amended claims.

1. (Amended) A method for transcutaneous immunization comprising:

- (a) providing a formulation comprised of at least one antigen and at least one adjuvant, wherein said at least one antigen or said at least one antigen is provided as at least one polynucleotide encoding said at least one antigen or said at least one adjuvant;
- (b) applying said formulation epicutaneously to skin of an organism without penetrating past dermis of said skin; and
- (c) inducing an antigen-specific immune response in said organism.

80. (Amended) A method for transcutaneous immunization of an organism comprising:

- (a) providing a formulation comprised of at least one antigen and at least one adjuvant, wherein said at least one antigen or said at least one antigen is provided as at least one polynucleotide encoding said at least one antigen or said at least one adjuvant and enhancement of immunologic activity by said adjuvant is separable from an immunogenic epitope of said antigen;
- (b) applying said formulation to skin of said organism; and
- (c) inducing an immune response in said organism specific for said immunogenic epitope which is enhanced as compared to a formulation that does not contain said adjuvant activity.

93. (Amended) A formulation which comprises:

- (a) at least one antigen, and

(b) at least one adjuvant;

wherein said at least one antigen or said at least one antigen is provided as at least one polynucleotide encoding said at least one antigen or said at least one adjuvant, enhancement of immunologic activity by said adjuvant is separable from an immunogenic epitope of said antigen, and said formulation induces an immune response specific for said immunogenic epitope which is enhanced as compared to a formulation that does not contain said adjuvant activity.

Kindly enter the following new claims.

102. (New) A method for inducing an immune response in an organism, the method comprising the steps of:
applying topically to skin of the organism an immunogen-encoding polynucleotide in an amount sufficient for uptake by a skin cell and sufficient for expression of the immunogen-encoding polynucleotide and induction of an immune response, wherein the skin to which the polynucleotide is applied comprises hair and is not treated with a chemical or mechanical penetration enhancer, and wherein the polynucleotide is operably linked to a promoter, and is not contained within a viral particle.

103. (New) The method of claim 102, wherein the skin to which the polynucleotide is applied is intact.

104. (New) The method of claim 102, wherein the polynucleotide is free of calcium phosphate.

105. (New) The method of claim 102, wherein the polynucleotide is administered in the absence of an amount of liposomes or cationic lipids effective to facilitate transfection.

106. (New) The method of claim 102, wherein the skin includes epidermis.

107. (New) The method of claim 102, wherein the organism is a mammal.

108. (New) The method of claim 102, wherein the organism is a human.

109. (New) The method of claim 102, wherein the immunogen-encoding polynucleotide is a polynucleotide encoding a polypeptide derived from a pathogen selected from the group consisting of bacterium, fungus, virus, and parasite.

110. (New) A method for inducing an immune response in an organism, the method comprising the steps of:
applying topically to skin of the organism an immunogen-encoding polynucleotide in an amount sufficient for uptake by a skin cell and sufficient for expression of the immunogen-encoding polynucleotide and induction of an immune response, wherein hair is not removed from the skin prior to applying the polynucleotide and the skin is not treated with a chemical or mechanical penetration enhancer, and wherein the polynucleotide is operably linked to a promoter and is not contained within a viral particle.

111. (New) The method of claim 110, wherein the skin includes epidermis.

112. (New) A method for introducing a polynucleotide into a skin cell in vivo for expression of a gene product encoded by the introduced polynucleotide, the method comprising the steps of:
applying topically to skin of a subject a polynucleotide in an amount sufficient for uptake by a skin cell and sufficient for expression of a gene product encoded by the polynucleotide to provide in the subject a biological effect associated with gene product expression; wherein the skin to which the polynucleotide is applied comprises hair and is not treated with a chemical or mechanical penetration enhancer, and wherein the polynucleotide is operably linked to a promoter, and is not contained within a viral particle.

113. (New) The method of claim 112, wherein the skin to which the polynucleotide is applied is intact.

114. (New) The method of claim 112, wherein the skin includes epidermis.

115. (New) A method for delivering a polypeptide to an organism, the method comprising the steps of:
applying topically to skin of the organism a polypeptide-encoding polynucleotide in an amount sufficient for uptake by a skin cell and sufficient for expression of the polypeptide to provide in the subject a biological effect associated with polypeptide expression; wherein the skin to which the polynucleotide is applied comprises hair and is not treated with a chemical or mechanical penetration enhancer, and wherein the polynucleotide is operably linked to a promoter, and is not contained within a viral particle.

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116. (New) The method of claim 115, wherein the polynucleotide is administered in the absence of an amount of liposomes or cationic lipids effective to facilitate transfection.

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